REMARKS

Claims 30, 32-33, and 35 have been canceled. Claims 31 and 34 have been amended and claims 46-50 have been added. No new matter has been inserted. Support for the limitation that the compound inhibits JAK-3 may be found throughout the specification and at least at the last paragraph on page 2. Support for the step of selecting an individual who is suffering from UVB-induced inflammation can be found at least at page 3, line 14. Claims 31, 34, and 46-50 are pending in this application. Applicants request entry of this Amendment and reconsideration of the claims.

35 U.S.C. § 102

Claims 30, 32, 33, and 35 remain rejected under 35 U.S.C. § 102(b) as being anticipated by Myers et al. (WO 95/15758). Applicants respectfully traverse this rejection.

The Applicants believe that the amendments to the claims obviate this rejection and further that Myers et al. is inapplicable to the newly added claims. However, to the extent the Examiner maintains this rejection, the following comments are made.

Myers teaches the use of compounds of a very broad genus for the inhibition of CSF-1R receptor tyrosine kinase activity. However, Myers does not teach inhibiting JAK-3 as required by independent claim 34. Nor does Myers teach administering to a mammal an effective amount of a JAK-3 inhibitor as required by independent claim 46. Further, Myers does not teach selecting a mammal that is suffering from UVB-induced inflammation as required by independent claim 47. Therefore, Myers does not anticipate claims 34 and 46-47. As claim 50 is dependent on claim 34, claims 31 and 49 are dependent on claim 46, and claim 48 is dependent on claim 47, these claims are also not anticipated.

For at least these reasons the Applicants respectfully request that this rejection be withdrawn.

35 U.S.C. § 103

Claims 30-35 are rejected under 35 U.S.C. § 103 as obvious over Myers et al. (WO 95/15758). The Applicants respectfully traverse this rejection.

The Applicants believe that the amendments to the claims obviate this rejection and further that Myers et al. is inapplicable to the newly added claims. However, to the extent the Examiner maintains this rejection, the following comments are made.

Myers teaches the use of compounds of a very broad genus for the inhibition of CSF-1R receptor tyrosine kinase. However, Myers does not teach that that the disclosed compounds inhibit JAK-3 as recited by independent claims 34 and 46 of the present invention. Further, Myers fails to suggest that compounds of the present invention inhibit JAK-3. The Examiner states that the distinction drawn by the Applicants regarding inhibition of CSF-1R in the prior art versus inhibition of JAK-3 in present application, although persuasive, is not particularly relevant in the nonobviousness analysis because the claims are not directed to subject matter of inhibition of JAK-3 or CSF-1R. Applicants submit that because independent claims 34 and 46 recite that the compound inhibits JAK-3 that this distinction is relevant and therefore Myers does not teach or suggest claims 34, 35, and 46. As claim 50 is dependent on claim 34, and claims 31 and 49 are dependent on claim 46, Myers also does not teach or suggest claims 31, 49, and 50.

Further, Myers does not teach or suggest selecting a mammal that is suffering from UVB-induced inflammation as recited by independent claim 47. Myers makes no suggestion as to this limitation. In fact, Myers only makes reference to treatment by broadly stating that the compounds disclosed "possess therapeutic value as cellular antiproliferative agents for the treatment of certain conditions including psoriasis, atherosclerosis and restenosis injuries," and that "compounds within the scope of the present invention exhibit the modulation and/or inhibition of cell signaling, cell proliferation, cell inflammatory response, the control of abnormal cell growth and can be used in preventing or delaying the occurrence or reoccurrence of such conditions or otherwise treating the condition." See p. 17. Accordingly, Myers does not teach or suggest selecting a mammal that is suffering from UVB-induced inflammation as recited by independent claim 47. As claim 48 is dependent on claim 47, it is also not taught or suggested by Myers.

Further, Myers does not teach or suggest the claims of the present invention because the disclosure of a genus of compounds is not sufficient to render all species falling within the genus *prima facie* obvious. MPEP 2144.08 provides the guidelines for the examination of claims directed to species of chemical compositions based upon a single prior art reference.

Under these guidelines, the Examiner must consider the size of the prior art genus. See MPEP 2144.08(a). The reference generically discloses tens of thousands of compounds (see Formula (I) page 4). Thus, the number of compounds disclosed by the reference is very large.

The Examiner must also consider the express teaching of the reference. See MPEP 2144.08(b). The compound testing in the reference was only preformed with: EGF-R and CSF-1R inhibition assays, and *lck* kinase and cAMP-dependent protein kinase (PKA) assays (see pages 17-23). There was absolutely no teaching regarding the inhibition of JAK-3. Thus, the express teaching of the reference does not provide any motivation to modify the reference to obtain the claimed invention.

The Examiner must also consider the properties of the prior art compounds. See MPEP 2144.08(d). It is the properties that provide real world motivation for a person of ordinary skill to make species structurally similar to those in the prior art. See *In re Dillion*, 919 F2d at 697. Large portions of the compounds generically disclosed in the reference are not structurally similar to the claimed compound. Further, in view of the disclosure regarding the structure required for JAK-3 inhibition, most of the compounds of Myers are highly unlikely to function as JAK-3 inhibitors.

The steps taken by the Applicants, as disclosed in the specification, reveal the structural specificity of a JAK-3 inhibitor. First, a homology model of the JAK-3 kinase domain was created. See Figs. 1B, 2A and pages 25-27, 32-34. The catalytic site was found to be a pocket located in the central region of the kinase domain, which is defined by two β-sheets at the interface between the N and C lobes. See p. 32. The opening of the catalytic site (a quadrilateral-shaped pocket) was found to be defined by residues Pro906, Ser907, Gly908, Asp912, Arg953, Gly829, Leu828, and Tyr904. The far wall deep inside the pocket was found to be lined with Leu905, Glu903, Met902, Lys905, and Asp967, and the floor of the pocket lined by Leu905, Val884, Leu956, and Ala966. The available volume in the pocket for binding was found to be approximately 530 cubic angstroms.

Using this detailed model, specific quinazoline compounds were made that were predicted to fit in the JAK-3 kinase active site. Such compounds were relatively planar, with dihedral angles of approximately 4-18 degrees between the phenyl ring and the quinazoline ring

system to allow the molecule to fit more easily into the catalytic site of JAK-3. See page 27, 34-36.

Next, these constructed compounds were used in JAK-3 kinase inhibition assays. The measured IC_{50} values were 9.1 μM for 4-(4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline, 11.0 μM for 4-(3'-5'-dibromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline, and 27.9 μM for 4-(3'-bromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline. See p. 36.

In sum, because of the precise structural characteristics required for a functional JAK-3 inhibitor, it is clear that the compounds broadly disclosed by Myers are unlikely to function as JAK-3 inhibitors. Therefore, the broad disclosure of thousands of compounds by Myers does not teach or suggest the claims of the present invention.

For at least these reasons the present claims are not disclosed or suggested by Myers. Withdrawal of this rejection is respectfully requested.

SUMMARY

Applicants submit the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicants' representative to clarify any of the above remarks or to otherwise speed prosecution of this application.

Respectfully submitted,

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MARKED-UP VERSION TO SHOW CHANGES MADE

Claims 30, 32-33, and 35 were canceled.

Claims 31 and 34 were amended as follows:

31. (Amended) The method of claim 46, [according to claim 30] wherein the compound is selected from the group consisting of:

4-(4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline,

4-(3'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline,

4-(3'-5'-dibromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline,

4-(3'-bromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline,

and pharmaceutically acceptable salts thereof.

34. (Amended) A method of inhibiting the release of prostaglandin E_2 in a mammal comprising inhibiting JAK-3 by administering to a mammal an effective amount of a compound [The method according to claim 33 wherein the compound is] selected from the group consisting of:

4-(4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline,

4-(3'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline,

4-(3'-5'-dibromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline,

4-(3'-bromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline,

and pharmaceutically acceptable salts thereof.

Claims 46-50 are new.